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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/092,063	03/05/2002	John Ford	28110/35908A	7957

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EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/092,063	FORD ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *05 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6/25/02* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *sequence alignment* .

DETAILED ACTION

1. Claim 1 is pending and being acted upon in this Office Action.

2. The references A11-A13 cited on PTO 1449 filed 6/25/02 have been considered but crossed out.

3. The disclosure is objected to because of the following informality: (1) (ATCC accession number ___) on page 8, line 11 and page 33, line 24 needs to be filled out. Appropriate action is required.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) an isolated polynucleotide comprising the nucleotide of SEQ IDNO: 2 that encodes a human apyrase and NDPase of SEQ ID NO: 3 for detection assays, **does not** reasonably provide enablement for (1) *any* isolated polynucleotide encoding an apyrase and/or NDPase and comprising any nucleotide sequence having at least about 80% sequence identity to a human polynucleotide selected from the group consisting of a polynucleotide having the nucleotide sequence having the nucleotide sequence of SEQ ID NO: 2 and any polynucleotide having the protein coding nucleotide sequence of the polynucleotide sequence of SEQ ID NO: 2 for treating a subject suffering from any disorder relating to thrombosis, coagulation or platelet aggregation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient

to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only a polynucleotide comprising a nucleotide sequence of SEQ ID NO: 2, encoding the amino acid sequence of SEQ ID NO: 3 which is a soluble apyrase, a vector comprising said polynucleotide, host cell comprising said vector, and a method of making a CD39L4 polypeptide. The specification further discloses a nucleotide sequence of the CD39L-4 mutant comprising SEQ ID NO: 6 that encodes the amino acid sequence of SEQ ID NO: 7 (Fig 6, in particular). The specification discloses that mutation in the ACR III increases ADPase activity over wild type (example 9, page 76) while mutations in ACR I and II eliminate apyrase activity.

The specification does not teach how to make and use *any* isolated polynucleotide encoding an apyrase and/or NDPase and comprising any nucleotide sequence having "at least about 80% sequence identity" to SEQ ID NO: 2 for treating any disease because (1) the minimal activity of "at least about 80% identity" is not clear. Even if the sequence is 80% identical to SEQ ID NO: 2 (1799 nucleotides), an 80% identity means 20% difference or (0.2 x 1799 = 359.8 nucleotides difference). (2) The term "having" is open-ended. IT expands the undisclosed polynucleotide to include additional nucleotides at either or both ends. (3) Since the nucleic acid sequence of a polynucleotide determines its protein coding properties, predicting which changes can be tolerated in a nucleic acid sequence and still retain similar functions and properties requires a knowledge of, and guidance as to which nucleotide(s) within the full-length polynucleotide of SEQ ID NO: 2 can tolerate modification such as substitution, deletion, and addition. There is insufficient guidance as to which nucleotide(s) within the full-length polynucleotide of SEQ ID NO: 2, the corresponding amino acids, can tolerate modification such as substitution, deletion, and addition and the resulting protein retains either apyrase activity, NDPase activity or both apyrase and NDPase activity. (4) With regard to "80% identity", although the specification teaches the use of the INHERIT TM 671 sequence analysis system to align nucleotide sequences, the specific parameters such as error tolerance are not disclosed. As such, it is inconceivable what parameters would be used to calculate the alignment of similar such as conservatively substituted amino acid residues even for 80% identity as recited in the claim. Given the lack of guidance in the assessment of 80% identity between two sequences, it is unpredictable to determine the metes and bound of the claimed sequence and whether such sequence has similar function even if it is identified.

It is known in the art that the relationship between the amino acid sequence of a protein (polypeptide) and its tertiary structure (i.e. its binding activity) are not well understood and are not predictable (see Ngo et al., in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz, et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495). Skolnick *et al* teach that sequence-based methods for function prediction are inadequate and knowing a protein's structure does not tell one its function (See abstract, in particular). Given the indefinite number of undisclosed polynucleotide that is at least about 80% identical to SEQ ID NO: 2, it is unpredictable which undisclosed polynucleotide encoding an apyrase, which undisclosed polynucleotide encodes NDPase and which undisclosed polynucleotide encodes an apyrase and NDPase. Since the polynucleotide is not enabled, the protein encoding by said undisclosed polynucleotide that is at least about 80% sequence identity to SEQ ID NO: 2 is not enabled.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

6. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) *any* isolated polynucleotide encoding an apyrase and/or NDPase and comprising any nucleotide sequence having at least about 80% sequence identity to a human polynucleotide selected from the group consisting of a polynucleotide having the nucleotide sequence having the nucleotide sequence of SEQ ID NO: 2 and any polynucleotide having the protein coding nucleotide sequence of the polynucleotide sequence of SEQ ID NO: 2 for treating a subject suffering from any disorder relating to thrombosis, coagulation or platelet aggregation.

The specification discloses only a polynucleotide comprising a nucleotide sequence of SEQ ID NO: 2, encoding the amino acid sequence of SEQ ID NO: 3 which is a soluble apyrase, a vector comprising said polynucleotide, host cell comprising said vector, and a method of making a CD39L4 polypeptide. The specification further discloses a nucleotide sequence of the CD39L-4 mutant comprising SEQ ID NO: 6 that encodes the amino acid sequence of SEQ ID NO: 7 (Fig 6, in particular). The specification discloses that mutation in the ACR III increases ADPase activity over wild type (example 9, page 76) while mutations in ACR I and II eliminate apyrase activity.

With the exception of the specific polynucleotide mentioned above for detection assays, there is inadequate written description about the structure associated with function of any polynucleotide encoding an apyrase and/or NDPase, any polynucleotide having at least about 80% sequence identity to SEQ ID NO: 2 because (1) the minimal activity of "at least about 80% identity" is not clear. Even if the sequence is 80% identical to SEQ ID NO: 2 (1799 nucleotides), an 80% identity means 20% difference or (0.2 x 1799 = 359.8 nucleotides difference). The specification discloses only one CD39L4 mutant comprising SEQ ID NO: 6. Further, the term "having" is open-ended. IT expands the undisclosed polynucleotide to include additional nucleotides at either or both ends. There is inadequate written description about which undisclosed polynucleotides, the corresponding amino acids, to be added and whether the resulting protein retains which function such as apyrase, NDPase or both apyrase and NDPase, in turn, useful for treating any disease. Given the lack of a written description of *any* additional representative species of polynucleotide encoding an apyrase, NDPase or both apyrase and NDPase comprising a nucleotide sequence having at least about 80% sequence identity to SEQ ID NO: 2, or the polynucleotide having the protein coding nucleotide sequence of SEQ ID NO: 2, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The "at least about 80% sequence identity" in claim 1 is indefinite and ambiguous because the minimum sequence identity is not clear. One of ordinary skill in the art cannot appraise the metes and bounds of the claimed invention.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

10. Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Chadwick *et al* (Mammalian Genome 8: 668-672, Sept 1997; PTO 1449).

Chadwick *et al* teach an isolated human polynucleotide comprising a nucleotide sequence having 87.5% identity to the claimed SEQ ID NO: 2, which is at least 80% sequence identity to the claimed SEQ ID NO: 2 (See Accession number AF039918, sequence alignment, in particular). The reference polynucleotide encodes a protein that inherently has apyrase activity since the reference protein sequence has high levels of amino acid sequence homology to the ecto-ATPase or apyrase-conserved regions (ACRs) (see page 668, column 1, in particular). Thus, the reference teachings anticipate the claimed invention.

11. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

12. Claim 1 is provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1 of copending Application No. 10/286,926. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

13. The non-statutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timeless extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cirri. 1993); *In re Long*, 759 F.2d 887, 225 USPQ 645 (Fed. Cirri. 1985); *In re Van Onramp*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970) and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claim 1 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 2, and 4-9 of USSN 10/286,916.

All of pending claims 2, and 4-9 of USSN 10/286,916 are drawn to nearly the same polynucleotide of instant claim 1. The issuance of a patent to instant application would encompass the pending claims 2, and 4-9 of USSN 10/286,916 for the following reasons.

(1) Claim 2 of USSN 10/286,916 recites a polynucleotide encoding an apyrase and/or NDPase and comprising a nucleotide sequence having at least about 90% identity to a human polynucleotide selected from the group consisting of (a) a polynucleotide having the nucleotide sequence of SEQ ID NO: 2 and (b) a polynucleotide having the protein coding nucleotide sequence of the polynucleotide sequence of (a), the issuance of a patent to USSN 10/092,063 would encompass the pending claim 2 of instant application because: the polynucleotide that is 90% identity to SEQ ID NO: 2 (claim 2 of USSN 10/286,916) is at least 80% identity to SEQ ID NO: 2 (claim 1 of instant application).

(2) Claim 4 of USSN 10/286,916 recites an isolated polynucleotide encoding a polypeptide with apyrase and/or NDPase activity that hybridizes under stringent conditions to the complement of a polynucleotide of SEQ ID NO: 2. The issuance of a patent to USSN 10/092,063 would encompass the pending claim 1 of instant application because: the isolated polynucleotide that hybridize to the complement of SEQ ID NO: 2 is the polynucleotide of SEQ ID NO: 2, which has at least 80% sequence identity to the SEQ ID NO: 2 of instant claim 1.

(3) Claim 5 of USSN 10/286,916 recites the polynucleotide mentioned above is a DNA. The issuance of a patent to USSN 10/092,063 would encompass the pending claim 1 of instant application because DNA is a species of polynucleotide (genus). The species anticipates a genus.

(4) Claim 6 of USSN 10/286,916 recites the polynucleotide mentioned above is a wholly or partially chemically synthesized DNA molecule. The issuance of a patent to USSN 10/092,063 would encompass the pending claim 1 of instant application because a product is a product, irrespective of how it is made.

(5) Claim 7 of USSN 10/286,916 recites an anti-sense polynucleotide which specifically hybridizes with the complement of the polynucleotide of an isolated polynucleotide encoding a polypeptide which apyrase and/or NDPase activity that hybridizes under stringent conditions to the complement of a polynucleotide of SEQ ID NO: 2. The issuance of a patent to USSN 10/092,063 would encompass the pending claim 1 of instant application because the antisense polynucleotide of USSN 10/286,916 would also hybridize to the polynucleotide of instant application since it is has at least 80% identity to SEQ ID NO: 2.

(6) Claim 8 of USSN 10/286,916 recites the polynucleotide encoding an apyrase and/or NDPase and comprising a nucleotide sequence having at least about 80% identity to a human polynucleotide selected from the group consisting of (a) a polynucleotide having the nucleotide sequence of SEQ ID NO: 2 and (b) a polynucleotide having the protein coding nucleotide sequence of the polynucleotide sequence of (a) which comprises the nucleotide sequence of SEQ IDNO: 2 or the mature protein coding portions thereof. The issuance of a patent to USSN 10/092,063 would encompass the pending claim 1 of instant application because the polynucleotide of SEQ ID NO: 2 of USSN 10/286,916 is the same polynucleotide of instant application.

(7) Claim 9 of USSN 10/286,916 recites an isolated polynucleotide which comprises a complement of polynucleotide encoding an apyrase and/or NDPase and comprising a nucleotide sequence having at least about 80% identity to a human polynucleotide selected from the group

consisting of (a) a polynucleotide having the nucleotide sequence of SEQ ID NO: 2 and (b) a polynucleotide having the protein coding nucleotide sequence of the polynucleotide sequence of (a). The issuance of a patent to USSN 10/092,063 would encompass the pending claim 1 of instant application because the complement of USSN 10/092,063 would also hybridizes to the polynucleotide that is 80% identity to SEQ ID NO: 2 of instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist (customer service) whose telephone number is (703) 872-9305.

17. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401. The IFW official Fax number is (703) 872-9306. For After Final, the Fax number is (703) 872-9307.

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